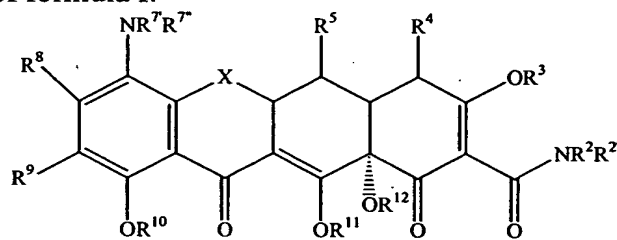


# CLAIMS

1. A compound of formula I:



(I)

wherein:

X is  $\text{CHC}(\text{R}^{13}\text{Y}'\text{Y})$ ,  $\text{CR}^6\text{R}^6$ , S,  $\text{NR}^6$ , or O;

$\text{R}^2$ ,  $\text{R}^4$ ,  $\text{R}^{4'}$ ,  $\text{R}^{7'}$  and  $\text{R}^{7''}$  are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$\text{R}^{2'}$ ,  $\text{R}^3$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$  and  $\text{R}^{12}$  are each hydrogen or a pro-drug moiety;

$\text{R}^4$  is  $\text{NR}^{4'}\text{R}^{4''}$ , alkyl, alkenyl, alkynyl, aryl, hydroxyl, halogen, or hydrogen;

$\text{R}^5$  is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$\text{R}^6$  and  $\text{R}^{6'}$  are independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

$\text{R}^8$  is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

$\text{R}^9$  is aminoalkyl;

$\text{R}^{13}$  is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

$\text{Y}'$  and  $\text{Y}$  are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl, and pharmaceutically acceptable salts, esters and prodrugs thereof.

2. The compound of claim 1, wherein  $\text{R}^4$  is  $\text{NR}^{4'}\text{R}^{4''}$ ; X is  $\text{CR}^6\text{R}^6$ ;  $\text{R}^2$ ,  $\text{R}^{2'}$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^{6'}$ ,  $\text{R}^8$ ,  $\text{R}^9$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$ , and  $\text{R}^{12}$  are each hydrogen; and,  $\text{R}^{4'}$ ,  $\text{R}^{4''}$ ,  $\text{R}^{7'}$ , and  $\text{R}^{7''}$  are each lower alkyl.

3. The compound of claim 2, wherein  $\text{R}^{4'}$ ,  $\text{R}^{4''}$ ,  $\text{R}^{7'}$ , and  $\text{R}^{7''}$  are each methyl.

4. The compound of claim 3, wherein said aminoalkyl is aminomethyl.

5. The compound of claim 3 or 4, wherein said aminoalkyl is substituted with an alkyl group.

6. The compound of claim 5, wherein said alkyl group is methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, or decyl.

7. The compound of claim 6, wherein said alkyl group is a branched chain alkyl group.

8. The compound of claim 5, wherein said alkyl group is n-pentyl.

9. The compound of claim 5, wherein said alkyl group has six carbon atoms or fewer.

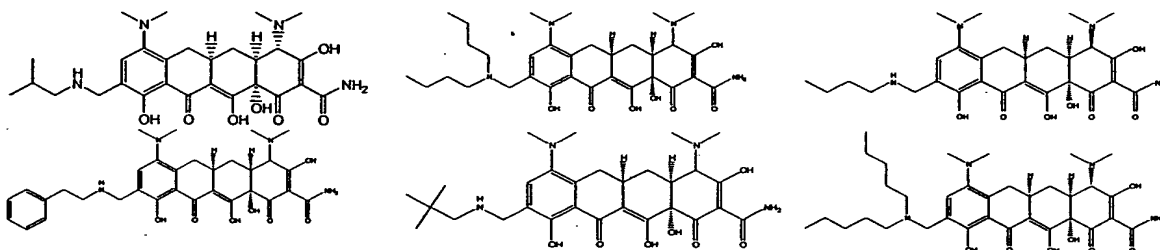
10. The compound of claim 5, wherein said alkyl group is unsubstituted.

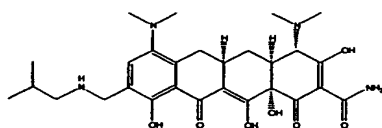
11. The compound of claim 5, wherein said alkyl group is substituted.

12. The compound of claim 11, wherein said alkyl group is substituted with alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, cyano, amino, acylamino, amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

13. The compound of claim 3, wherein said aminoalkyl is substituted with two alkyl groups.

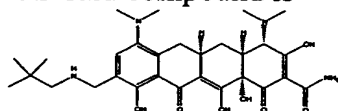
14. The compound of claim 5, wherein said compound is selected from the group consisting of:





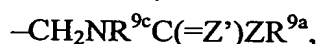
or pharmaceutically acceptable salts, esters and prodrugs thereof.

15. The compound of claim 5, wherein said compound is



5 or pharmaceutically acceptable salts, esters and prodrugs thereof.

16. The compound of claim 3, wherein said aminoalkyl is of the formula



wherein

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Z is  $\text{CR}^{9d}\text{R}^{9e}$ , S,  $\text{NR}^{9b}$  or O;

Z' is  $\text{NR}^{9f}$ , O or S; and

$\text{R}^{9a}$ ,  $\text{R}^{9b}$ ,  $\text{R}^{9c}$ ,  $\text{R}^{9d}$ ,  $\text{R}^{9e}$  and  $\text{R}^{9f}$  are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

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17. The compound of claim 16, wherein  $\text{R}^{9c}$  is hydrogen.

18. The compound of claim 16, wherein Z' is S, NH, or O.

20

19. The compound of claim 16, wherein Z is  $\text{NR}^{9b}$ , O or S.

20. The compound of claim 19, wherein  $\text{R}^b$  is hydrogen or alkyl.

21. The compound of claim 16, wherein  $\text{R}^a$  is an aryl group.

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22. The compound of claim 21, wherein  $\text{R}^a$  is unsubstituted phenyl, *para*-nitrophenyl, *para*-methoxy phenyl, *para*-perfluoromethoxy phenyl, *para*-acetyl phenyl, 3, 5-methylenedioxyphenyl, 3,5-diperfluoromethyl phenyl, *para*-bromo phenyl, *para*-chloro phenyl, or *para*-fluoro phenyl.

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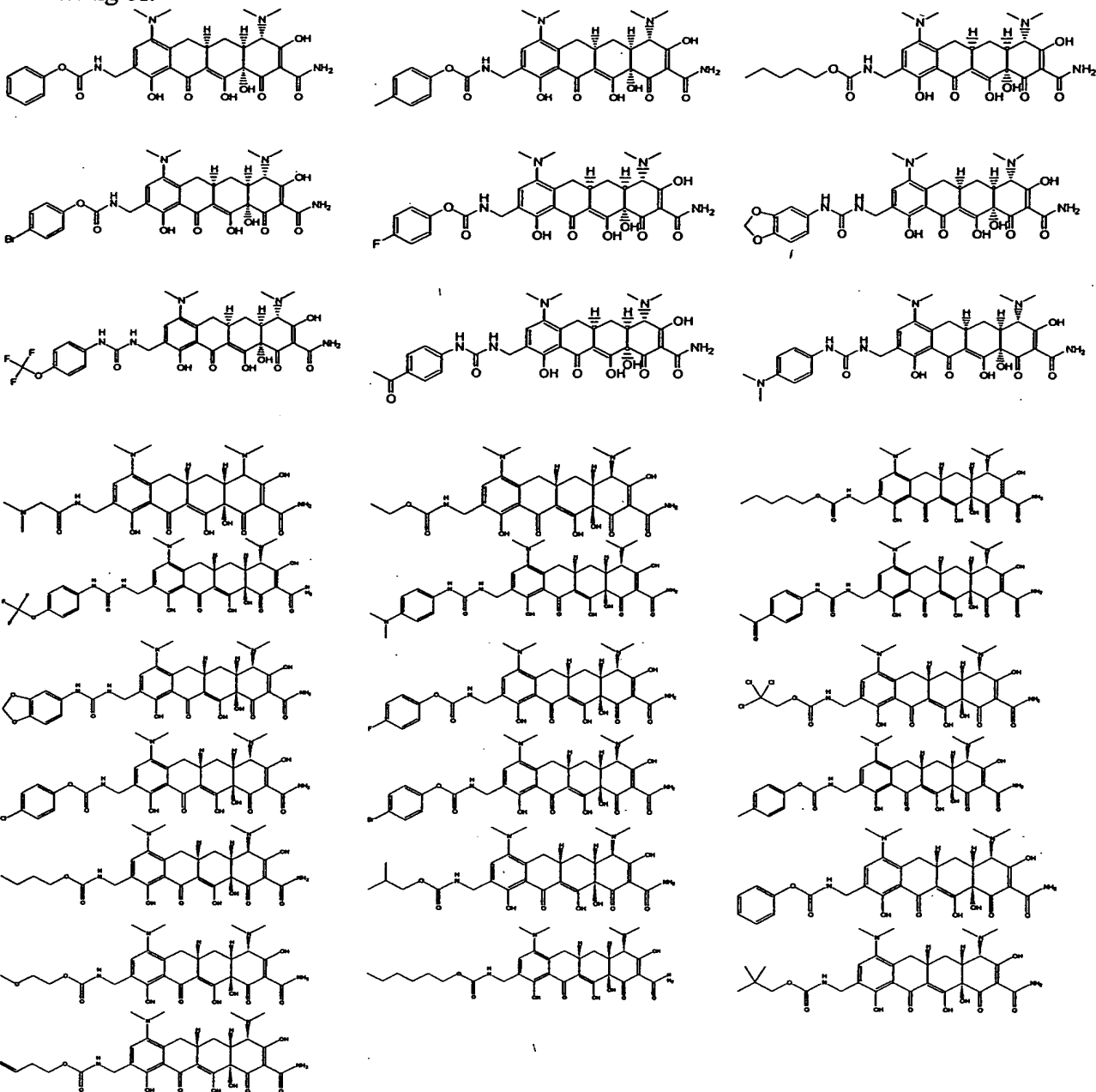
23. The compound of claim 21, wherein  $\text{R}^{9a}$  is a heterocycle.

24. The compound of claim 16, wherein  $\text{R}^{9a}$  is substituted or unsubstituted alkyl.

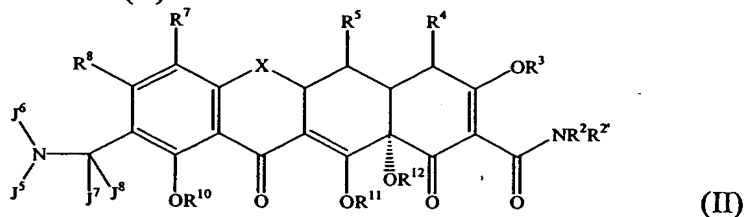
25. The compound of claim 16, wherein R<sup>9a</sup> is substituted or unsubstituted alkenyl.

26. The compound of claim 16, wherein said compound is selected from the group consisting of:

5



27. A compound of formula (II):



**wherein:**

J<sup>5</sup> and J<sup>6</sup> are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, sulfonyl, acyl, alkoxycarbonyl, alkaminocarbonyl, alkaminothiocarbonyl, substituted thiocarbonyl, substituted carbonyl, alkoxythiocarbonyl, or linked to form a ring;

$J^7$  and  $J^8$  are each alkyl, halogen, or hydrogen;

X is  $\text{CHC}(\text{R}^{13}\text{Y}'\text{Y})$ ,  $\text{CR}^6\text{R}^6$ ,  $\text{C}=\text{CR}^6\text{R}^6$ , S,  $\text{NR}^6$ , or O;

R<sup>2</sup>, R<sup>2'</sup>, R<sup>4'</sup>, and R<sup>4''</sup> are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^4$  is  $NR^{4'}R^{4''}$ , alkyl, alkenyl, alkynyl, aryl, hydroxyl, halogen, or hydrogen;

**R<sup>2'</sup>, R<sup>3</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each hydrogen or a pro-drug moiety;**

R<sup>5</sup> is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$R^6$  and  $R^{6'}$  are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R<sup>7</sup> and R<sup>8</sup> and are each independently hydrogen, dialkylamino, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R<sup>13</sup> is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl, and pharmaceutically acceptable salts thereof.

28. The compound of claim 27, wherein R<sup>4</sup> is NR<sup>4'</sup>R<sup>4''</sup>, X is CR<sup>6</sup>R<sup>6'</sup>; R<sup>2</sup>, R<sup>2'</sup>, R<sup>6</sup>, R<sup>6'</sup>, R<sup>8</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are each hydrogen; R<sup>4'</sup> and R<sup>4''</sup> are lower alkyl; R<sup>7</sup> is dialkylamino; and R<sup>5</sup> is hydroxy or hydrogen.

29. The compound of claim 28, wherein R<sup>4'</sup> and R<sup>4''</sup> are each methyl and R<sup>5</sup> is hydrogen.

30. The compound of claim 28, wherein J<sup>7</sup> and J<sup>8</sup> are hydrogen.

31. The compound of claim 28, wherein J<sup>5</sup> is substituted or unsubstituted alkyl.

5 32. The compound of claim 32, wherein J<sup>5</sup> is branched alkyl.

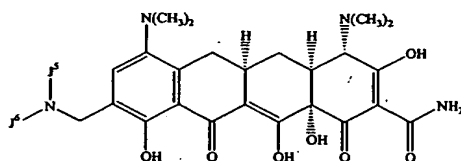
33. The compound of claim 32, wherein J<sup>5</sup> is pentyl.

34. The compound of claim 33, wherein J<sup>5</sup> is n-pentyl.

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35. The compound of claim 33, wherein J<sup>6</sup> is hydrogen.

36. A compound of the formula (III):



15

(III)

wherein

J<sup>5</sup> is alkyl; and

J<sup>6</sup> is hydrogen, or pharmaceutically acceptable salts, prodrugs and esters thereof.

20 37. The compound of claim 36, wherein J<sup>5</sup> is n-pentyl.

38. A method for treating a tetracycline responsive state in a mammal, comprising administering to said subject a compound of claim 1, 15, 27, or 36, such that said subject is treated.

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39. The method of claim 38, wherein said tetracycline responsive state is a bacterial infection.

40. The method of claim 39, wherein said bacterial infection is associated with gram positive bacteria.

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41. The method of claim 39, wherein said bacterial infection is associated with gram negative bacteria.

35 42. The method of claim 39, wherein said bacterial infection is associated with *E. coli*.

43. The method of claim 39, wherein said bacterial infection is associated with *S. aureus*.

44. The method of claim 39, wherein said bacterial infection is associated with *E. faecalis*.

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45. The method of claim 39, wherein said bacterial infection is resistant to other tetracycline antibiotics.

46. The method of claim 38, wherein said compound is administered with a  
10 pharmaceutically acceptable carrier.

47. The method of claim 38, wherein said subject is a human.

48. A pharmaceutical composition comprising a therapeutically effective amount of a  
15 compound of claims 1, 15, 27, or 36 and a pharmaceutically acceptable carrier.